

Protocol Title: Comparative study between behavior therapy and
behavior therapy plus mirabegron 50mg in sexually
active men with bothersome overactive bladder
symptoms – A multicenter, randomized study

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1. OBJECTIVE AND ENDPOINTS

The objective of this study is to evaluate and compare the therapeutic effects on OAB symptoms, and sexual functions, in terms of erectile function and ejaculatory function, in sexually active OAB male treated with behavior therapy or behavior therapy plus Mirabegron (50 mg).

The primary and secondary endpoints are described as shown below:

(1) Primary End-point (3 months)

Change from baseline in OABSS, and IIEF-5 (International Index of Erectile Function) at Week 12.

(2) Secondary end-points

Efficacy

1. Change from baseline in OABSS, IIEF-5 and MSHQ-EjD (Male Sexual Health Questionnaire - Ejaculatory Domain) Short Form at Week 4, and MSHQ-EjD Short Form at Week 12.
2. Net change of the following parameters from baseline to 1 and 3 months after the treatment day: (1) Frequency episode, nocturia episode, urgency episode, UII episodes in 3-day voiding diary, (2) maximum flow rate (Qmax), voided volume, and postvoid residual (PVR) volume, (3) IPSS symptom score and PPBC, from baseline to 1 and 3 months.
3. Global response assessment (GRA) of satisfaction by the patient (categorized into -3, -2, -1, 0, 1, 2, 3, indicating markedly worse to markedly improved) at 1 and 3 months after the treatment day. An improvement of GRA by 2 scales is considered effective.

Safety

- (1) Local adverse event incidences (hematuria, miction pain, UTI, urinary retention). The severity of adverse event is categorized as indicated below:

<i>Severity of AE</i>	<i>Description</i>
Mild	Transient and easily tolerable, not affecting usual daily activities
Moderate	Causes patient's discomfort, interrupting usual daily activities
Severe	Causes considerable interference with daily activities and may be incapacitating or life-threatening

(2) Randomization

Permuted block randomization method will be applied to generate randomization codes. Each randomization number will be assigned to individual patient according to the time-sequence for screened patient become eligible. This is a prospective, multi-center, randomized, open label study in sexually active male OAB patients treated with behavior therapy alone or behavior therapy plus mirabegron 50mg OD in a 1:2 ratio.

(3) Blinding

This study is not a blinded study.

2. SUBJECTS

2.1. Number and Source

This study will be conducted at Kaohsiung Chang Gung Memorial Hospital, and 4 other medical centers. Approximately 150 patients will be enrolled and completed within the two-year study period.

2.2. Inclusion Criteria

Patients must meet all the following criteria to be eligible to enter the trial:

- 2.2.1. Sexually active men with OAB ≥ 20 year.
- 2.2.2. Diagnosed with OAB based on OABSS (OABSS urgency score of ≥ 2 and sum score of ≥ 3).
- 2.2.3 Patients can sign informed consent and record voiding diary.

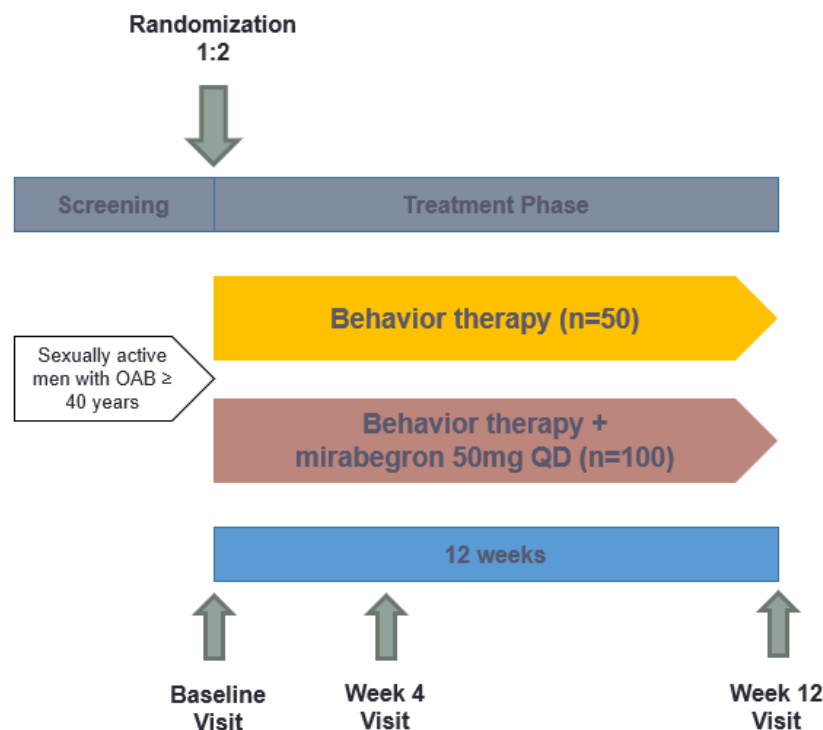
2.3. Exclusion Criteria

- 2.3.1. Concurrent use of PDE5 inhibitor or testosterone therapy during study period.
- 2.3.2. History of stress urinary incontinence.
- 2.3.3. Neurologic conditions associated with OAB symptoms.
- 2.3.4. Evidence of active urinary tract infection or urinary tract stone at screening.

- 2.3.5. Confirmed or suspected genitourinary tract or pelvic malignancy.
- 2.3.6. Genitourinary tract operation during the 3-month period prior to baseline.
- 2.3.7. Postvoid residual urine volume (PVR) ≥ 100 mL.
- 2.3.8. History of uncontrolled hypertension (systolic >180 mmHg and/or diastolic >110 mmHg).
- 2.3.9. History of intolerance to mirabegron.
- 2.3.10. History of medical conditions or presence of patient factors that, in the judgement of the investigator, would preclude adherence to study protocol.
- 2.3.11. Patient had received intravesical onabotulinumoxinA treatment within recent 6 months.

3. STUDY PROCEDURE

Patients who fulfill the inclusion criteria and sign informed consent will be randomized to behavior therapy or behavior therapy plus mirabegron 50mg OD (by the central study nurse) and followed up at 1 month, and 3 months (primary end-point).



Behavior therapies [1]:

1. reduction of fluid intake at specific times aimed at reducing urinary frequency when most inconvenient (e.g. at night or when going out in public);
2. avoidance/moderation of intake of caffeine or alcohol, which may have a diuretic and irritant effect, thereby increasing fluid output and enhancing frequency, urgency and nocturia;
3. use of relaxed and double-voiding techniques;
4. urethral milking to prevent post-micturition dribble;
5. distraction techniques such as penile squeeze, breathing exercises, perineal pressure, and mental tricks to take the mind off the bladder and toilet, to help control storage symptoms;
6. bladder retraining that encourages men to hold on when they have sensory urgency to increase their bladder capacity and the time between voids;
7. reviewing the medication and optimising the time of administration or substituting drugs for others that have fewer urinary effects (these recommendations apply especially to diuretics);
8. providing necessary assistance when there is impairment of dexterity, mobility or mental state;
9. treatment of constipation.

REFERENCES

1. URL: <https://uroweb.org/guideline/treatment-of-non-neurogenic-male-luts/>
Management of Non-neurogenic Male LUTS. European Association of Urology, 2019 Guidelines.